

Fig. 1

2/18

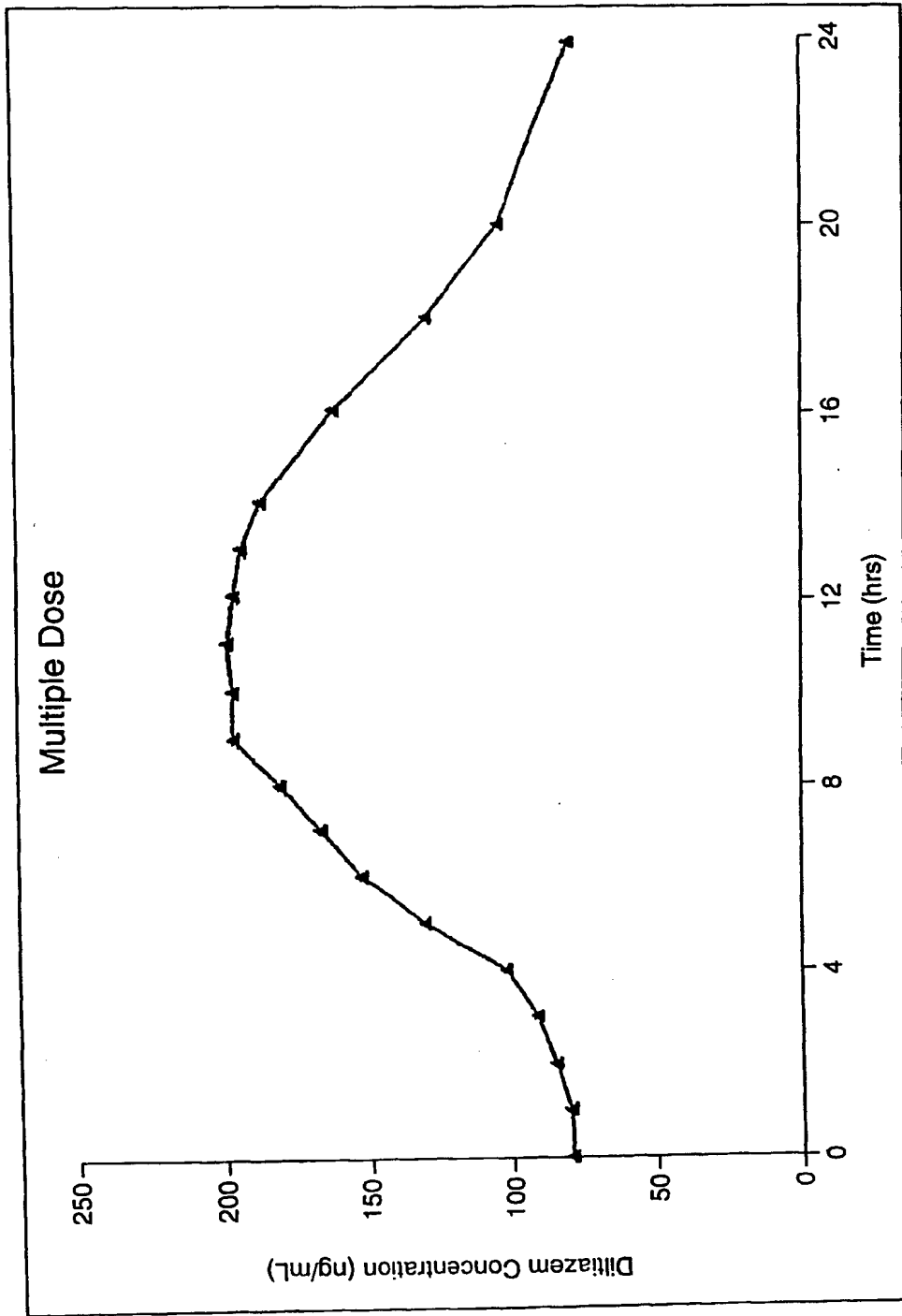


Fig. 2

3/15

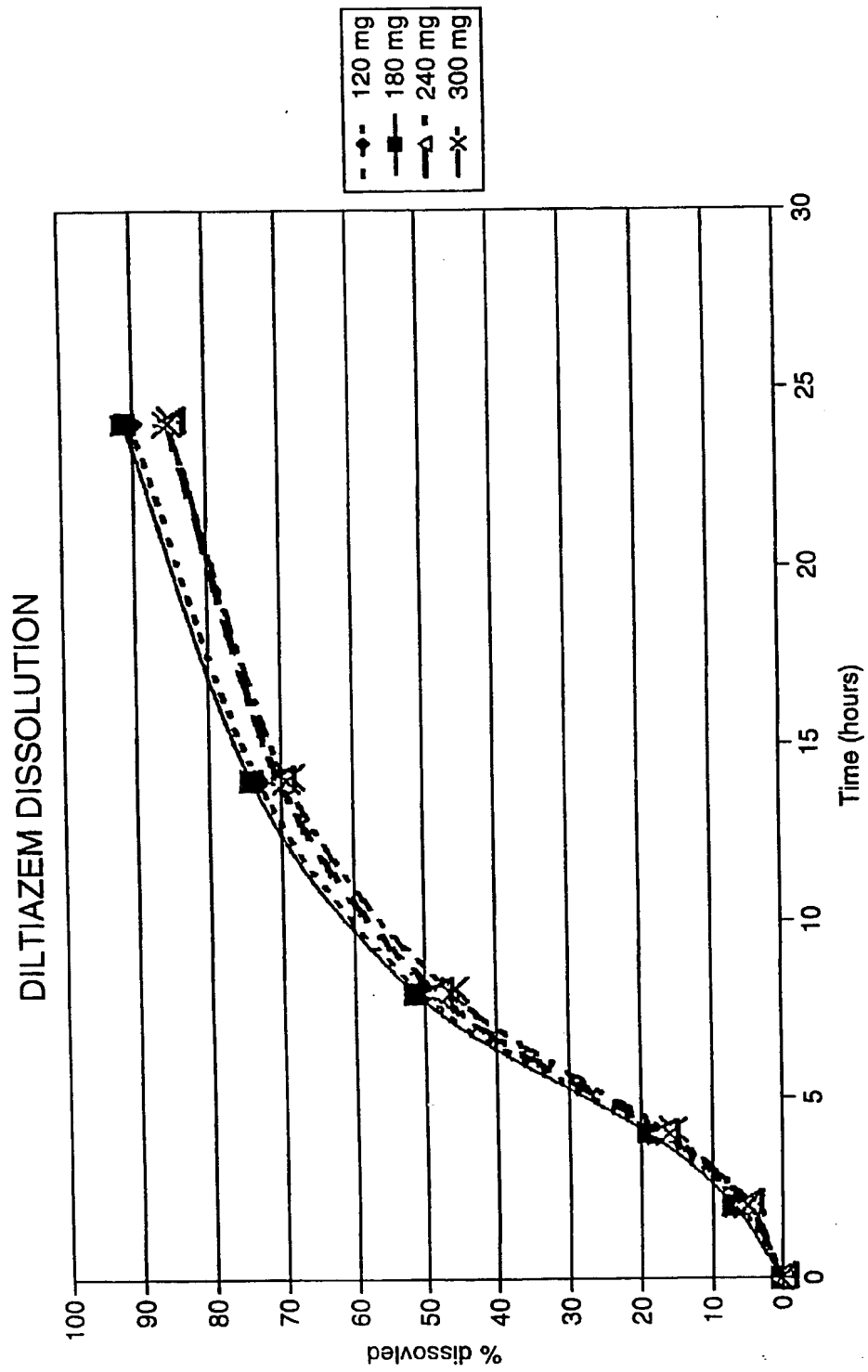


Fig. 3

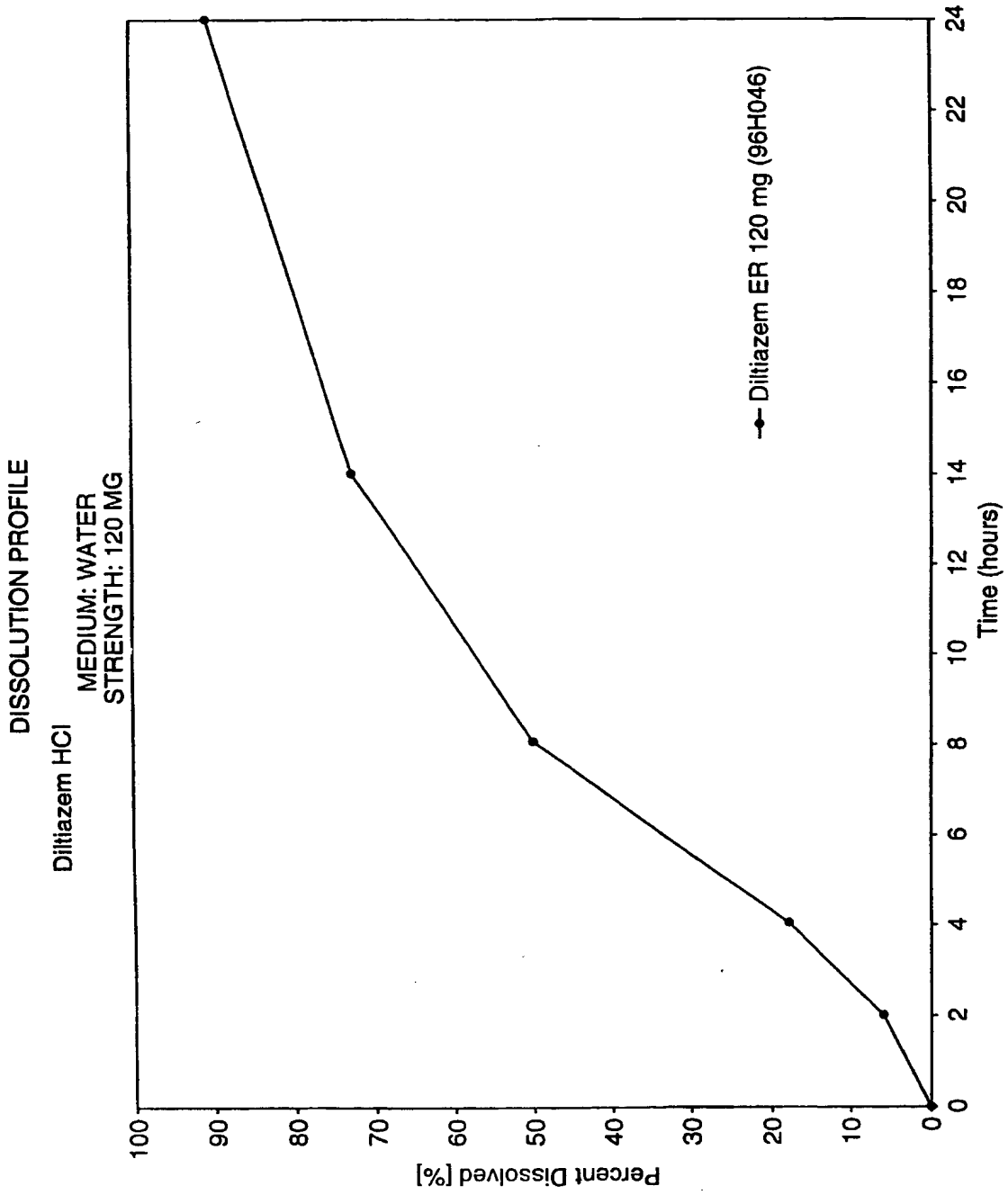


Fig. 4

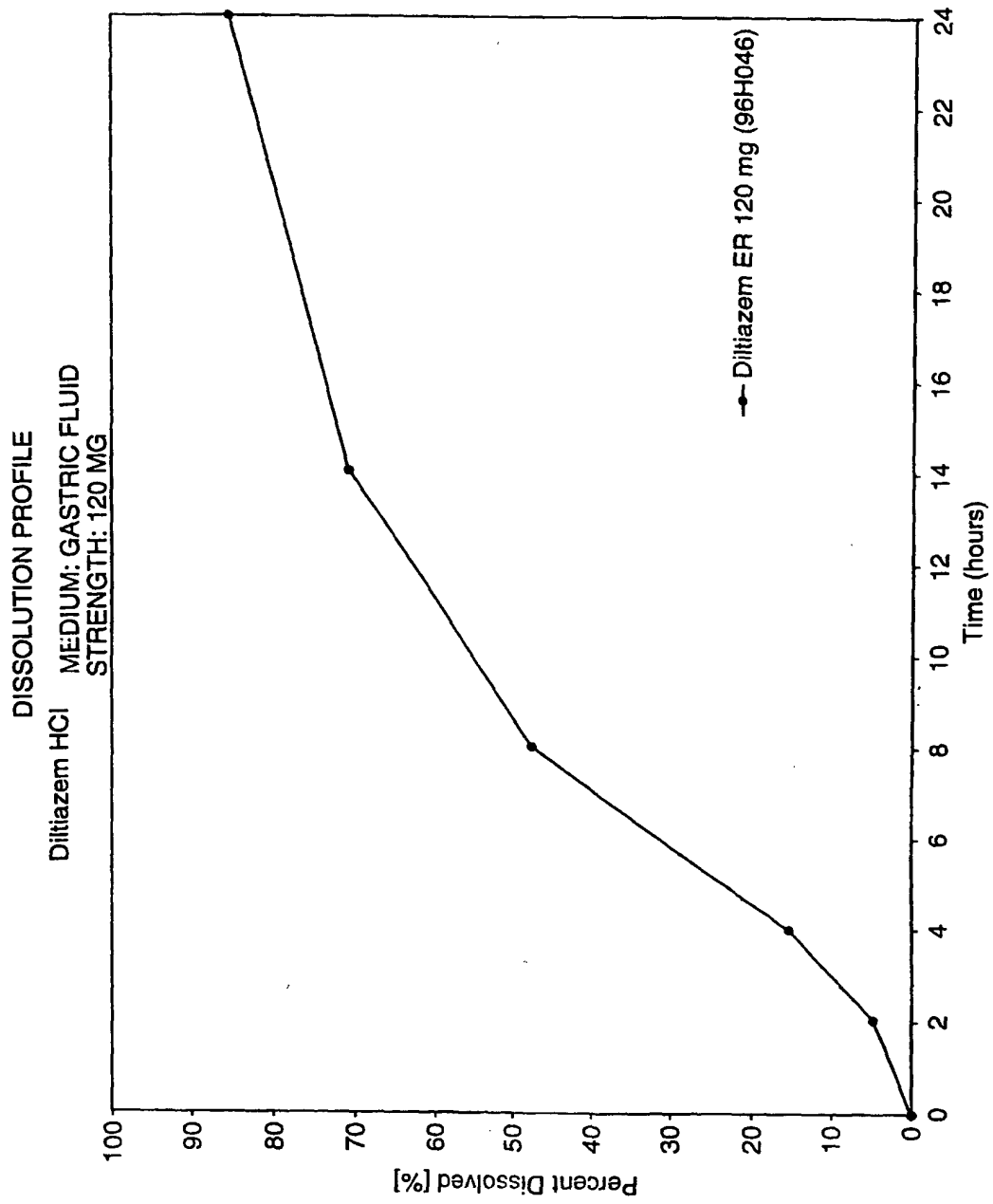


Fig. 5

6/18

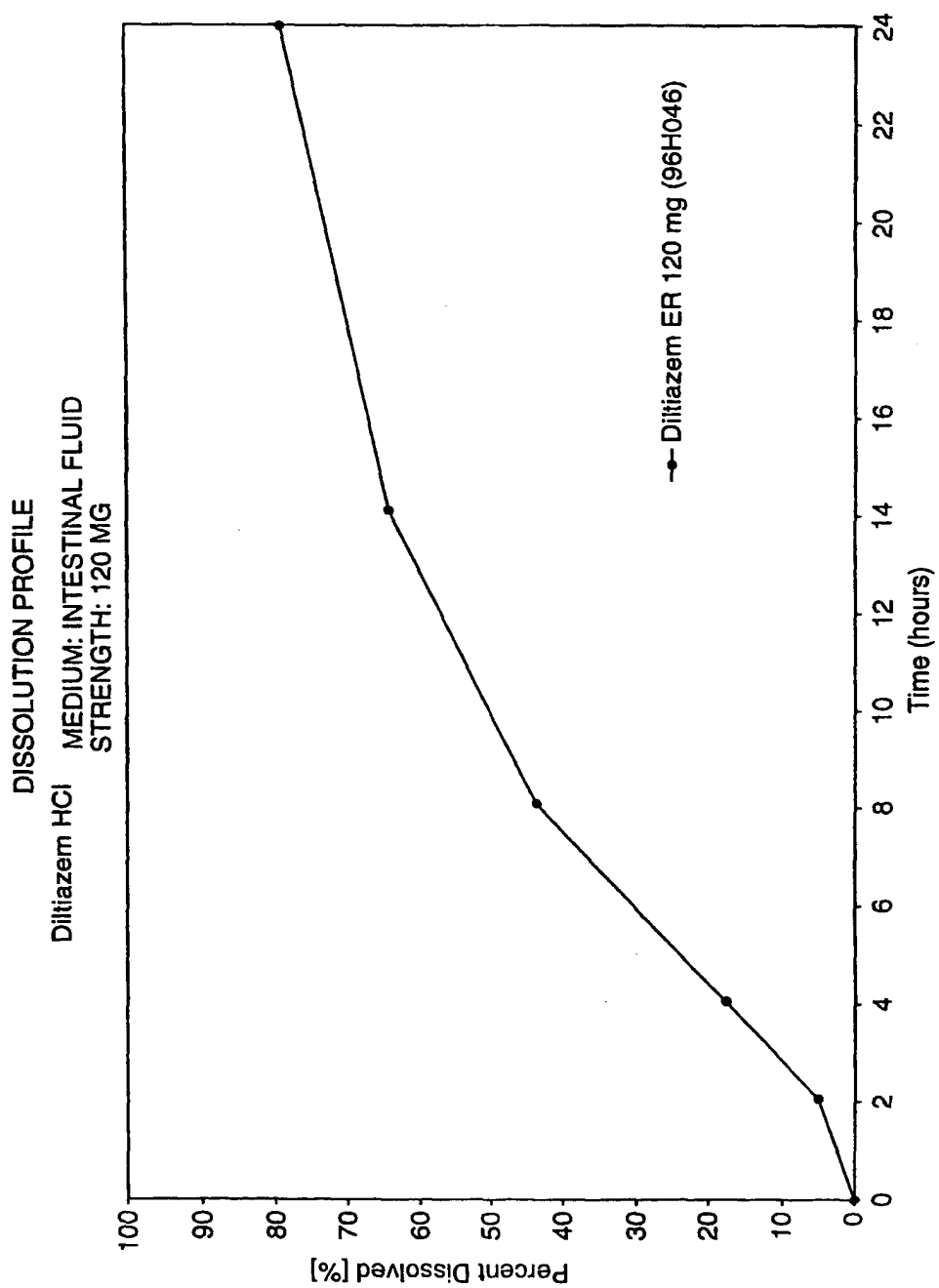


Fig. 6

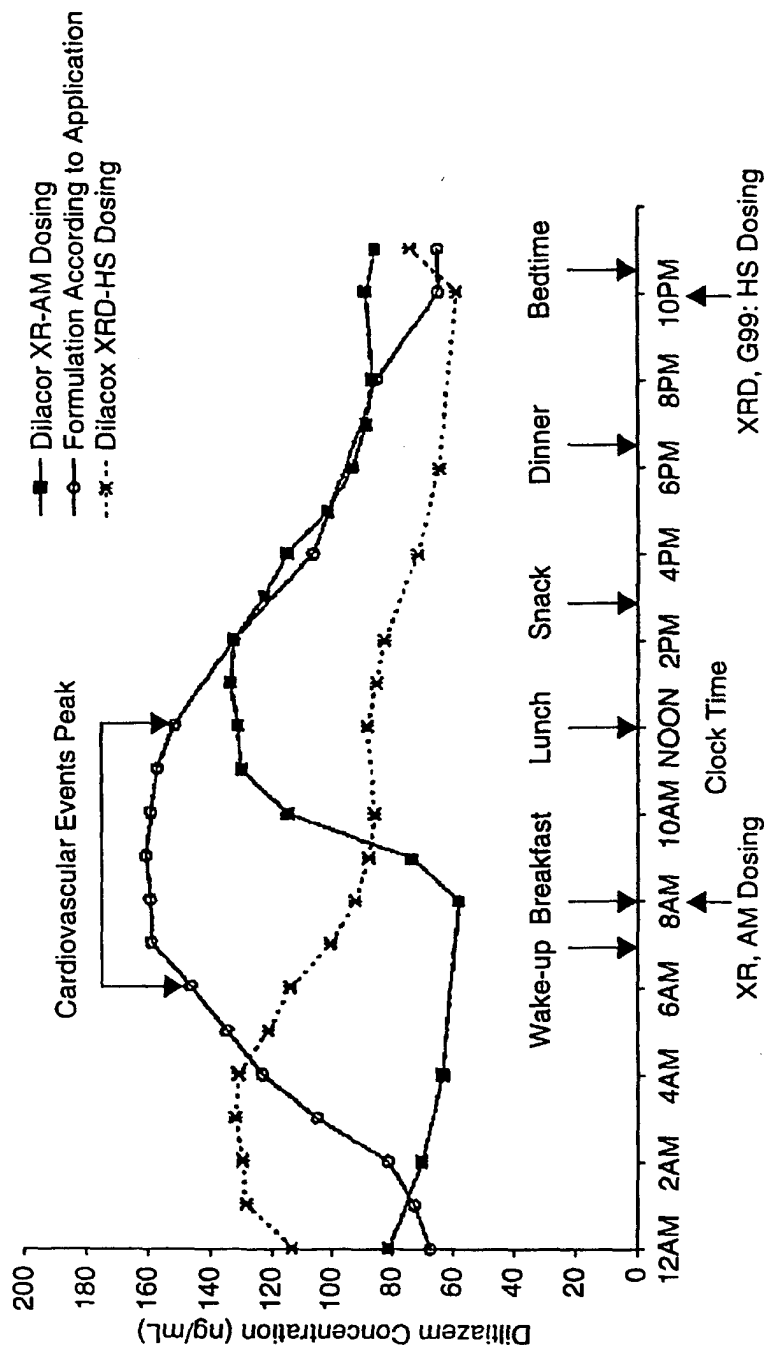


Fig. 7

8/18

■ Tiazac  
○ Formulation  
According to  
Application

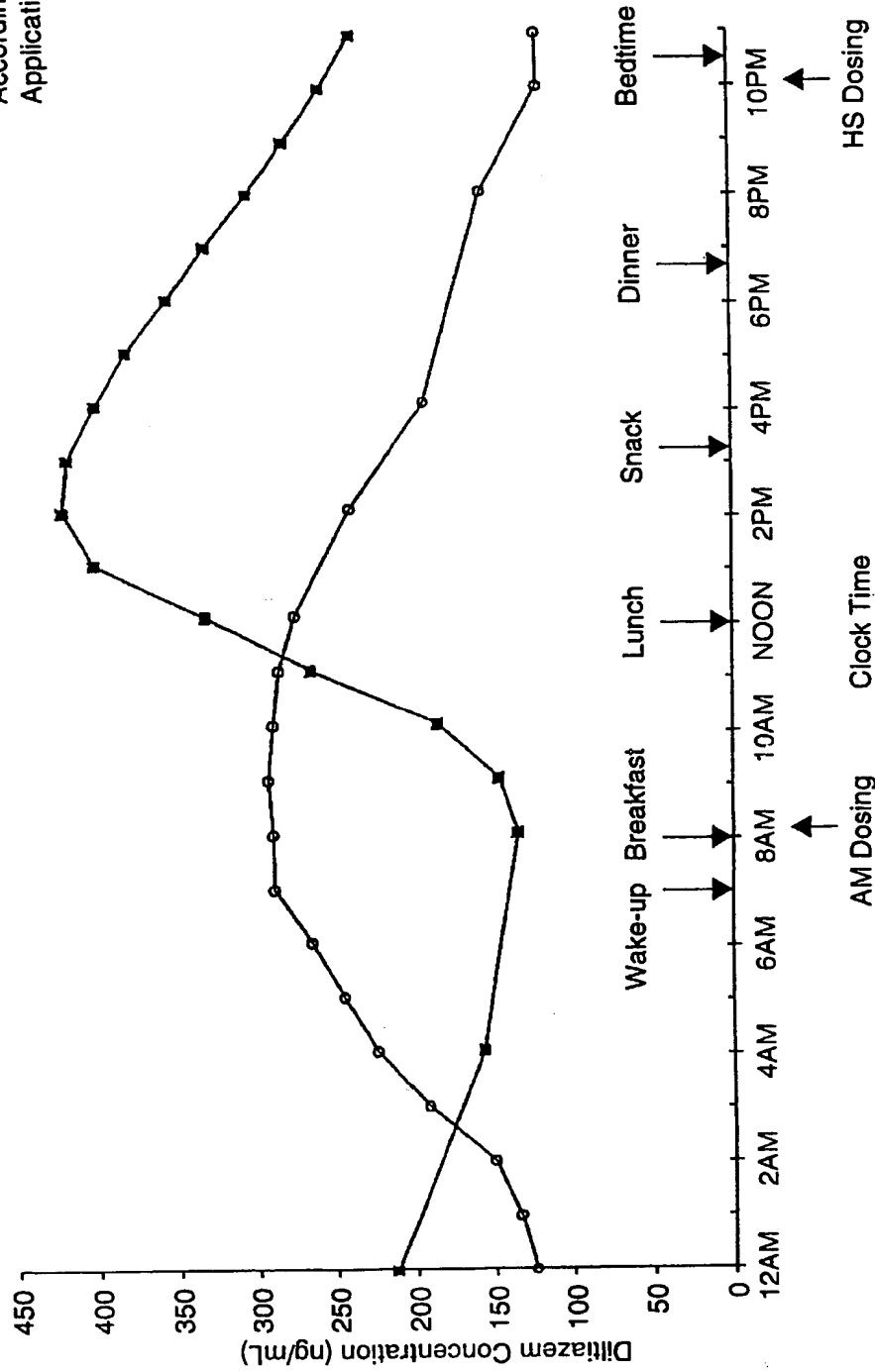


Fig. 8

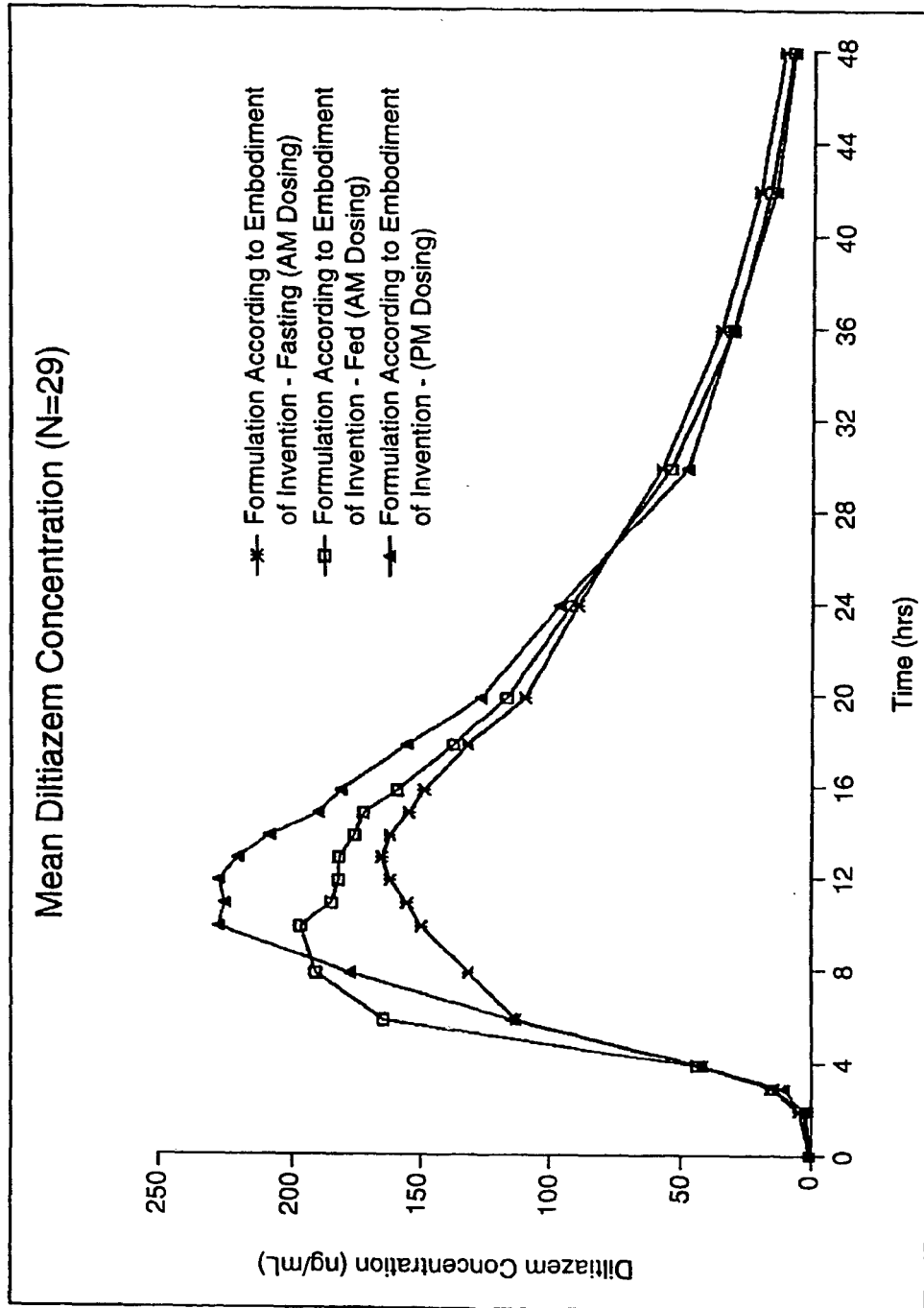


Fig. 9

10/18

**Diltiazem AUCt PK Summary**

**Formulation According to Embodiment of Invention**

Formulation According to Enrichment of Invention							Morning	
Subject	Morning Fasting		Morning Fed		Night Dosing		Fed/Fast	Night/Morning
	AUCt	Log AUCt	AUCt	Log AUCt	AUCt	Log AUCt	Ratio	Ratio
2	1730.75	7.46	2647.15	7.88	1987.11	7.59	1.53	1.15
3	2712.98	7.91	2336.67	7.76	3249.94	8.09	0.88	1.20
4	2688.34	7.90	1907.61	7.55	2892.21	7.97	0.71	1.08
5	4192.37	8.34	4108.85	8.32	4702.33	8.46	0.98	1.12
6	3074.51	8.03	2887.98	7.97	3900.06	8.27	0.94	1.27
7	1629.81	7.40	1847.56	7.52	2723.36	7.91	1.13	1.67
8	941.10	6.85	1970.97	7.59	1835.11	7.51	2.09	1.95
9	3144.13	8.05	3462.59	8.15	2923.86	7.98	1.10	0.93
10	2074.94	7.64	2997.45	8.01	4028.83	8.30	1.44	1.94
11	3653.96	8.20	2771.53	7.93	3464.72	8.15	0.76	0.95
12	2684.22	7.90	3790.43	8.24	3141.47	8.05	1.41	1.17
13	3352.69	8.12	3751.95	8.23	3708.83	8.22	1.12	1.11
14	2988.61	8.00	3665.60	8.21	3141.05	8.05	1.23	1.05
15	6796.97	8.82	8204.22	9.01	7578.33	8.93	1.21	1.11
16	2873.70	7.96	4644.79	8.44	4182.09	8.34	1.62	1.46
17	4468.33	8.40	4222.55	8.35	3762.50	8.23	0.94	0.84
18	5654.29	8.64	5635.72	8.64	7159.38	8.88	1.00	1.27
19	4944.07	8.51	5107.44	8.54	4812.20	8.48	1.03	0.97
20	2986.73	8.00	2988.34	8.00	2791.23	7.93	1.00	0.93
21	2908.88	7.98	3314.12	8.11	4389.98	8.39	1.14	1.51
22	4270.43	8.36	3790.06	8.24	3631.01	8.20	0.89	0.85
23	6150.18	8.72	6092.56	8.71	7478.22	8.92	0.99	1.22
25	2926.46	7.98	5633.64	8.64	4839.10	8.48	1.93	1.65
26	3928.61	8.28	4614.43	8.44	4359.77	8.38	1.17	1.11
27	3637.94	8.20	4587.48	8.43	4063.15	8.31	1.26	1.12
28	4177.76	8.34	4945.31	8.51	6689.14	8.81	1.18	1.60
29	3609.69	8.19	2720.67	7.91	2163.20	7.68	0.75	0.60
30	4483.17	8.41	5222.54	8.66	5587.50	8.63	1.16	1.25
32	4058.04	8.31	3531.47	8.17	3082.87	8.03	0.87	0.76
Mean	3542.88	8.10	3910.40	8.21	4078.57	8.25	1.15	1.20
SD	1304.23	0.41	1431.24	0.36	1554.69	0.37	0.33	0.33
CV	36.81	5.08	36.60	4.43	38.12	4.46	28.23	27.33
Median	3352.69	8.12	3751.95	8.23	3762.50	8.23	1.12	1.12
Geo Mean	3292.83	8.09	3671.24	8.20	3818.30	8.24	1.11	1.16
Fed/Fasting Ratio (Morning Dosing)								
Ratio of Means		1.10	#	Ratio of Means				1.15
Ratio of Geo Means		1.11	#	Ratio of Geo Means				1.16
Avg of Individual Ratios		1.15	#	Avg of Individual Ratios				1.20

**Fig. 9A**

11/18

Diltiazem Cmax PK Summary

Formulation According to Embodiment of Invention

Subject	Morning Fasting			Morning Fed			Night Dosing			Morning	
	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	Fed/Fast Ratio	Night/Morning Ratio
2	10.0	98.63	4.59	10.0	187.71	5.23	13.0	143.84	4.97	1.90	1.48
3	13.0	136.18	4.91	11.0	123.04	4.81	10.0	246.57	5.51	0.90	1.81
4	15.0	133.23	4.89	10.0	118.68	4.78	10.0	191.44	5.25	0.89	1.44
5	8.0	222.52	5.41	8.0	185.68	5.28	12.0	254.98	5.54	0.88	1.15
6	12.0	150.95	5.02	8.0	164.11	5.10	16.0	178.67	5.19	1.09	1.19
7	10.0	90.68	4.51	14.0	121.64	4.80	12.0	179.87	5.19	1.34	1.98
8	8.0	85.68	4.18	11.0	119.30	4.78	11.0	133.35	4.89	1.82	2.03
9	13.0	155.46	5.05	6.0	292.70	5.88	12.0	175.62	5.17	1.88	1.13
10	8.0	95.45	4.56	6.0	168.91	5.12	13.0	196.94	5.28	1.75	2.06
11	14.0	212.41	5.36	11.0	154.64	5.04	14.0	183.68	5.21	0.73	0.86
12	10.0	117.75	4.77	10.0	201.43	5.31	11.0	174.95	5.16	1.71	1.49
13	14.0	149.90	5.01	13.0	188.51	5.24	10.0	208.78	5.34	1.26	1.39
14	13.0	139.54	4.94	6.0	205.35	5.32	13.0	187.32	5.23	1.47	1.34
15	16.0	268.48	5.59	15.0	330.93	5.80	13.0	450.34	8.11	1.24	1.89
16	13.0	134.55	4.90	8.0	281.74	5.64	10.0	236.10	5.48	2.08	1.75
17	12.0	224.85	5.41	10.0	244.82	5.50	14.0	203.51	5.32	1.09	0.91
18	14.0	281.88	5.64	8.0	308.25	5.73	13.0	479.11	8.17	1.09	1.70
19	15.0	227.89	5.43	11.0	262.82	5.57	13.0	231.49	5.44	1.15	1.02
20	14.0	137.54	4.82	10.0	175.78	5.17	10.0	173.93	5.16	1.28	1.26
21	13.0	164.75	5.10	13.0	197.83	5.29	13.0	301.72	5.71	1.20	1.83
22	16.0	182.52	5.21	11.0	207.19	5.33	10.0	247.08	5.51	1.14	1.35
23	18.0	269.97	5.60	10.0	340.21	5.83	10.0	500.82	8.22	1.28	1.86
25	10.0	166.06	5.11	8.0	322.55	5.78	10.0	263.27	5.57	1.94	1.59
26	13.0	208.19	5.34	10.0	237.50	5.47	10.0	235.12	5.46	1.14	1.13
27	10.0	162.47	5.09	8.0	255.85	5.54	10.0	170.18	5.14	1.57	1.05
28	13.0	218.59	5.39	11.0	236.10	5.46	11.0	384.02	5.95	1.08	1.76
29	13.0	215.15	5.37	13.0	160.73	5.08	12.0	129.94	4.87	0.75	0.60
30	14.0	242.88	5.49	12.0	244.58	5.50	10.0	338.64	5.82	1.01	1.39
32	12.0	303.43	5.72	15.0	204.09	5.32	11.0	231.33	5.44	0.67	0.76
Mean	12.6	176.45	5.12	10.2	215.53	5.33	11.6	242.48	5.42	1.29	1.41
SD	2.5	61.85	0.37	2.5	64.85	0.31	1.8	98.98	0.38	0.40	0.39
CV	19.8	34.66	7.32	24.3	30.09	5.83	14.1	40.82	6.58	30.89	27.83
Median	13.0	164.75	5.10	10.0	204.09	5.32	11.0	208.76	5.34	1.20	1.39
Geo Mean	12.3	167.47	5.11	9.9	206.00	5.32	11.5	226.83	5.41	1.23	1.35
Fed/Fasting Ratio (Morning Dosing)											Night/Morning Ratio
Ratio of Means											1.36
Ratio of Geo Means											1.35
Avg of Individual Ratios											1.41

Fig. 9B

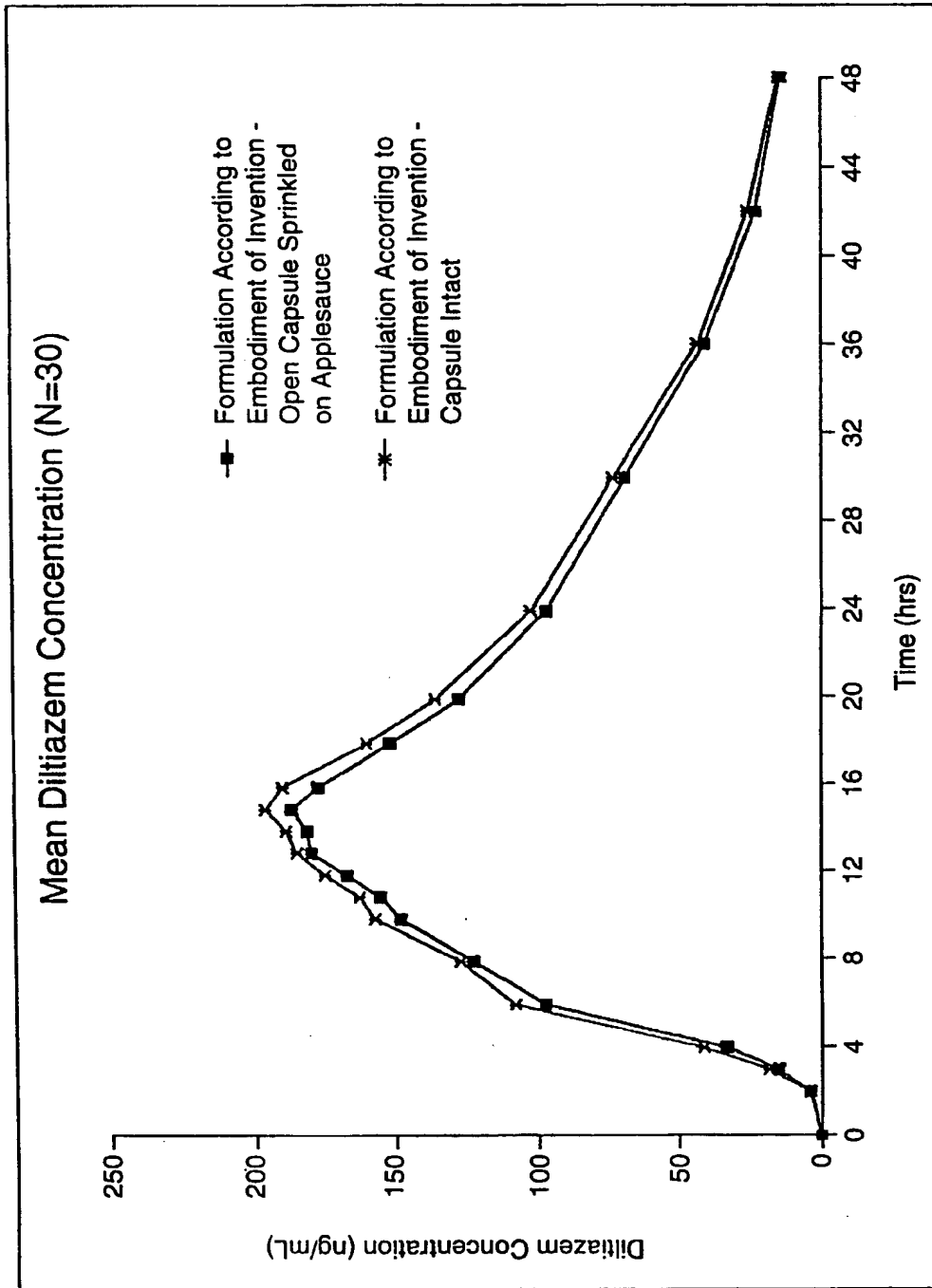


Fig. 10

PK Summary (N=30)

Diltiazem PK

Open Capsule Sprinkled on Applesauce / Capsule Intact

AUCt

Ratio of Means % 94.16  
 Ratio of Geo Means % 93.98  
 Avg of Individual Ratios % 96.03  
 90% C.I. 88%-99%  
 Intra-CV 13.47%

Cmax

Ratio of Means % 93.35  
 Ratio of Geo Means % 93.00  
 Avg of Individual Ratios % 95.73  
 90% C.I. 86%-99%  
 Intra-CV 16.07%

Imax

Open Capsule Sprinkled on Applesauce  
 Capsules Intact

Mean

13.7 hours  
 13.5 hours

Fig. 10A

14/18

**Diltiazem AUCt Results**

**Formulation According to Embodiment of Invention**

Subject	Open Capsules Sprinkled on Applesauce (A)		Capsule Intact (B)		(A:B) Ratio
	AUCt	Log Cmax	AUCt	Log Cmax	
1	3937.18	8.28	3251.62	8.09	1.21
2	3792.89	8.24	5502.18	8.61	0.69
3	1616.35	7.39	2358.22	7.77	0.69
4	8209.44	9.01	7954.29	8.98	1.03
5	2171.26	7.68	2452.78	7.80	0.89
6	5710.90	8.65	7082.30	8.87	0.81
7	1983.56	7.59	2624.03	7.87	0.76
8	3862.46	8.26	3114.53	8.04	1.24
9	6069.65	8.71	4585.60	8.43	1.32
10	3907.33	8.27	6393.14	8.76	0.61
11	3842.58	8.25	4292.30	8.36	0.90
12	4873.82	8.49	6493.87	8.78	0.75
13	2707.85	7.90	3922.90	8.27	0.69
14	2553.27	7.85	2159.88	7.68	1.18
15	2042.47	7.62	2902.70	7.97	0.70
16	4650.14	8.44	4769.32	8.47	0.98
17	3705.72	8.22	3464.89	8.15	1.07
19	7881.69	8.97	6851.45	8.83	1.15
21	6151.00	8.72	6292.65	8.75	0.98
22	2138.64	7.67	1933.52	7.57	1.11
23	3983.50	8.29	5177.74	8.55	0.77
24	3939.51	8.28	3517.56	8.17	1.12
25	2318.36	7.75	2016.26	7.61	1.15
27	2061.09	7.63	1928.02	7.56	1.07
28	2871.31	7.96	3312.87	8.11	0.87
29	4305.14	8.37	3559.57	8.18	1.21
30	3190.17	8.07	3565.88	8.18	0.89
31	3422.16	8.14	3012.17	8.01	1.14
33	4906.47	8.50	5206.52	8.56	0.94
34	2969.19	8.00	3255.28	8.09	0.91
Mean	3859.17	8.17	4098.47	8.24	0.96
SD	1664.90	0.42	1708.24	0.41	0.20
CV	43.14	5.10	41.68	5.03	20.69
Median	3817.74	8.25	3538.57	8.17	0.96
Geo Mean	3546.16	8.16	3773.43	8.23	0.94
Test/Ref Ratio					
Ratio of Means %		94.16			
Ratio of Geo Means %		93.98			
Avg of Individual Ratios		0.96			
90% C.I.		88%-99%			
Intra-CV		13.47%			

**Fig. 10B**

15/18

**Diltiazem Cmax Results**

**Formulation According to Embodiment of Invention**

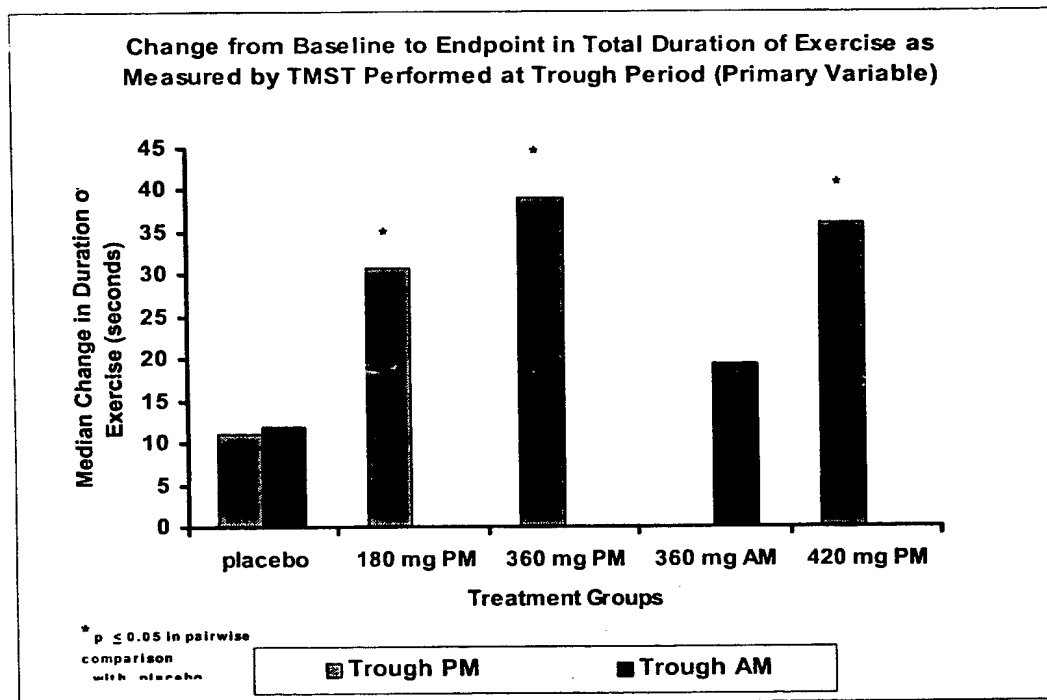
Subject	Open Capsule Sprinkled on Applesauce (A)			Capsule Intact (B)			(A:B) Ratio
	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	
1	13.0	184.35	5.22	13.0	228.99	5.43	0.81
2	14.0	192.44	5.26	12.0	286.72	5.66	0.67
3	13.0	103.87	4.64	12.0	127.07	4.84	0.82
4	10.0	372.93	5.82	8.0	298.05	5.70	1.25
5	14.0	107.71	4.68	16.0	147.84	5.00	0.73
6	13.0	244.87	5.50	15.0	315.48	5.75	0.78
7	14.0	115.23	4.75	16.0	135.27	4.91	0.85
8	13.0	257.26	5.55	15.0	179.11	5.19	1.44
9	8.0	232.12	5.45	10.0	194.37	5.27	1.19
10	16.0	172.20	5.15	15.0	281.81	5.64	0.61
11	13.0	177.41	5.18	8.0	181.17	5.20	0.98
12	13.0	225.55	5.42	10.0	327.23	5.79	0.69
13	15.0	135.86	4.91	15.0	213.37	5.36	0.64
14	15.0	154.65	5.04	14.0	135.94	4.91	1.14
15	12.0	114.81	4.74	15.0	181.80	5.20	0.63
16	15.0	294.21	5.68	13.0	296.58	5.69	0.99
17	15.0	187.32	5.23	15.0	183.62	5.21	1.02
19	16.0	385.36	5.95	15.0	376.57	5.93	1.02
21	15.0	318.06	5.76	10.0	276.15	5.62	1.15
22	14.0	114.40	4.74	14.0	97.24	4.58	1.18
23	12.0	260.20	5.56	12.0	346.74	5.85	0.75
24	14.0	211.61	5.35	16.0	202.88	5.31	1.04
25	14.0	155.98	5.05	15.0	125.66	4.83	1.24
27	16.0	79.66	4.38	16.0	67.35	4.21	1.18
28	16.0	124.76	4.83	16.0	165.01	5.11	0.76
29	15.0	225.58	5.42	10.0	164.02	5.10	1.38
30	14.0	166.54	5.12	15.0	165.41	5.11	1.01
31	15.0	134.14	4.90	14.0	135.19	4.91	0.99
33	13.0	282.10	5.64	16.0	275.33	5.62	1.02
34	10.0	118.88	4.78	15.0	155.15	5.04	0.77
Mean	13.7	195.00	5.19	13.5	208.90	5.27	0.96
SD	1.9	80.09	0.41	2.5	80.27	0.41	0.23
CV	13.8	41.07	7.83	18.3	38.43	7.73	24.25
Median	14.0	180.88	5.20	15.0	182.71	5.21	0.99
Geo Mean	13.5	180.09	5.18	13.3	193.65	5.25	0.83
Test/Ref Ratio							
Ratio of Means %			93.35				
Ratio of Geo Means %			93.00				
Avg of Individual Ratios			0.96				
90% C.I.			86%-99%				
Intra-CV			16.07%				

**Fig. 10C**

16/18

5

FIGURE 11



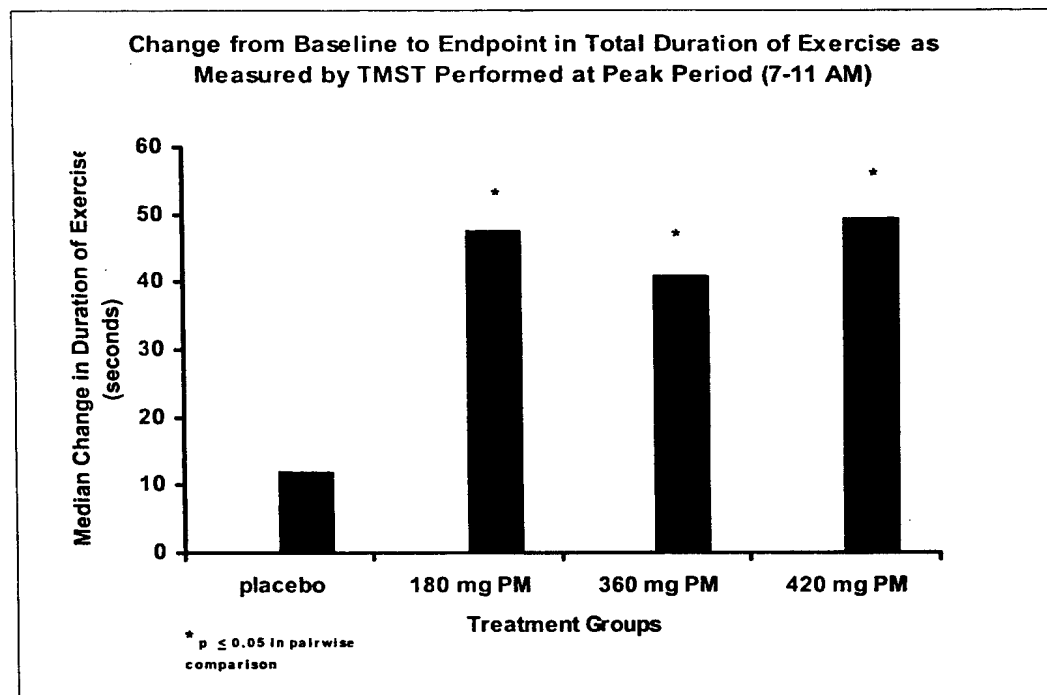
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15

17/18

FIGURE 12

5



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15

18/18

FIGURE 13

5

